RD2008-09

Registration Decision

Fluazinam

(publié aussi en français)

10 November 2008

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

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ISBN: 978-1-100-10510-9 (978-1-100-10511-6)
Catalogue number: H113-25/2008-9E (H113-25/2008-9E-PDF)

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Overview

Registration Decision for Fluazinam

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is granting full registration for the sale and use of Technical Fluazinam Fungicide and Allegro 500F Agricultural Fungicide containing the technical grade active ingredient fluazinam to control late blight on potatoes.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

These products were first proposed for registration in the consultation document[1]: Proposed Registration Decision, PRD2008-08, *Fluazinam*. This Registration Decision[2] describes this stage of the PMRA's regulatory process for fluazinam and summarizes the Agency's decision and the reasons for it. The PMRA received no comments on PRD 2008-08 that would impact the risk assessment. This decision is consistent with the proposed registration decision stated in PRD2008-08.

For more details on the information presented in this Registration Decision, please refer to Proposed Registration Decision PRD2008-08, which contains a detailed evaluation of the information submitted in support of this registration.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions of registration.[3] The Act also requires that products have value[4] when used according to label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

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1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

3 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

4 "Value" as defined by subsection 2(1) of *Pest Control Products Act* "...the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (a) efficacy; (b) effect on host organisms in connection with which it is intended to be used; and (c) health, safety and environmental benefits and social and economic impact."

To reach its decisions, the PMRA applies modern, rigorous risk assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (e.g. children) as well as organisms in the environment (e.g. those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties present when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the PMRA's website at www.pmra-arla.gc.ca.

What Is Fluazinam?

Fluazinam is the active ingredient in Allegro 500F Agricultural Fungicide. This preventative fungicide is a contact fungicide that acts on the surface of the plant to control late blight on potatoes.

Health Considerations

Can Approved Uses of Fluazinam Affect Human Health?

Fluazinam is unlikely to affect your health when used according to the label directions.

Exposure to fluazinam may occur through diet (food and water) or when handling and applying the product. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human populations (e.g. children and nursing mothers).

Only those uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100 times higher (and often much higher) than levels to which humans are normally exposed when using fluazinam products according to label directions.

Fluazinam caused thyroid tumours in male rats and liver tumours in male mice. However, these tumour types seen in the respective rodents studied are rarely seen in the general human population. There was also no indication that fluazinam caused damage to the nervous system. The first signs of toxicity in animals given daily doses of fluazinam over longer periods of time were effects on body weight, liver, uterus and blood chemistry. The risk assessment protects against these effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

When fluazinam was given to pregnant animals, effects on the developing fetus were observed at doses that were toxic to the mother, though the effects observed were more severe, indicating the fetus was more sensitive to fluazinam than the adult animal. Also, potentially endocrine-related effects were seen in the two-year mouse study. Consequently, extra protective measures were applied during the risk assessment to further reduce the allowable level of human exposure to fluazinam.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Reference doses define levels to which an individual can be exposed over a single day (acute) or lifetime (chronic) and expect no adverse health effects. Generally, dietary exposure from food and water is acceptable if it is less than 100% of the acute reference dose or chronic reference dose (acceptable daily intake). An acceptable daily intake is an estimate of the level of daily exposure to a pesticide residue that, over a lifetime, is believed to have no significant harmful effects.

Dietary intake estimates (food plus water) revealed that children and adults including seniors will typically consume less than 2% of the acceptable daily intake for fluazinam. Infants, the segment of the population that would ingest the most fluazinam relative to body weight, are expected to be exposed to less than 2% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from fluazinam is not a concern for all population subgroups.

New animal studies resulted in revisions to the acute toxicological endpoints. The aggregate (food and water) dietary intake estimate for females of childbearing age (13 to 49 years old) and the total population (including infants and children) based on these revised endpoints were each less than 7% of the acute reference dose, which is not a health concern.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act.* Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in or on certain foods. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

The residue trials submitted to support the registration of Allegro 500F Agricultural Fungicide on potatoes were conducted throughout Canada and the United States using end-use products containing fluazinam. These trials were sufficient to propose an MRL for potatoes and processed food derived from potatoes. This MRL can be found in the Science Evaluation of the Proposed Registration Decision, PRD2008-08, *Fluazinam.*

Occupational Risks From Handling Fluazinam

Occupational risks are not of concern when Allegro 500F Agricultural Fungicide is used according to the label directions, which include protective measures.

The label will specify that anyone mixing, loading or applying Allegro 500F Agricultural Fungicide or performing clean-up or repair activities must wear coveralls over a long-sleeved shirt and long pants, shoes plus socks and chemical-resistant gloves. Taking into consideration these label requirements, the risk to workers handling Allegro 500F Agricultural Fungicide is not of concern.

Environmental Considerations

What Happens When Fluazinam Is Introduced Into the Environment?

Fluazinam presents a risk to freshwater and marine aquatic organisms. It also poses a dietary and reproductive risk to wild mammals. Therefore, buffer zones are required to protect sensitive aquatic habitats when fluazinam is applied. In addition, an environmental hazard statement based on the persistence and high carryover of fluazinam must be added to the label of the end-use product, Allegro 500F, to protect sensitive organisms.

Fluazinam enters the environment when used as a fungicide on potatoes. Fluazinam is moderately persistent in soil. Both fluazinam and the metabolite HYPA are expected to significantly carry over into the next field season. Although the use pattern of fluazinam does not include direct application to bodies of water, the possibility that aquatic systems may be exposed to fluazinam, directly or indirectly, cannot be ruled out. Although fluazinam does not persist in aquatic systems, its major transformation product, CAPA, is stable to hydrolysis in the aquatic environment.

Laboratory and field studies indicate that fluazinam and its major transformation products will not leach through the soil.

Based on its low vapour pressure and Henry's law constant, fluazinam is considered to be non-volatile in the environment. Fluazinam residues are, therefore, not expected in the air and long-range transport is not expected.

Fluazinam presents a negligible risk to earthworms, honeybees, wild birds, sediment-dwelling organisms and marine/estuarine fish. Fluazinam is expected to adversely affect the vegetative vigour of terrestrial vascular plants, the dietary and reproductive capacity of wild mammals, freshwater invertebrates (acute and chronic basis), freshwater fish (acute, chronic and reproductive basis), freshwater algae and aquatic vascular plants (acute basis), and marine invertebrates. Therefore, buffer zones and environmental hazard statements on the toxicity of fluazinam to both aquatic and terrestrial organisms were placed on the product label.

Value Considerations

What Is the Value of Allegro 500F Agricultural Fungicide?

Allegro 500F Agricultural Fungicide provides effective control of potato late blight (*Phytophthora infestans*) when applied at 200 g a.i./ha, in 200–600 litres of water per hectare and applied at 7- to 10-day intervals. The level of disease control is similar to other commercial standards that are currently registered for this disease.

The value in registering Allegro 500F Agricultural Fungicide is that it provides Canadian potato growers with an alternative product to control potato late blight. It can be applied up to 10 times throughout the growing season, which may be necessary for season-long control of this disease as late blight can occur at any time during crop production. Allegro 500F Agricultural Fungicide is a Group 29 fungicide containing the active ingredient fluazinam, which has been identified as having a low risk of leading to resistance development. The use of Allegro 500F Agricultural Fungicide will give potato growers a new product with a different mode of action that can be used in rotation with existing chemical control methods and may replace applications of older fungicide chemistries.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures on the label of Allegro 500F Agricultural Fungicide to address the potential risks identified in this assessment are as follows.

Human Health

- As there is a concern with users coming into direct contact with fluazinam or Allegro 500F Agricultural Fungicide, hazard statements have been added to the product label to communicate potential hazards to the users.

- Anyone mixing, loading or applying Allegro 500F Agricultural Fungicide or performing clean-up or repair activities must wear coveralls over a long-sleeved shirt and long pants, shoes plus socks and chemical-resistant gloves.

Environment

The following statement must be included on the Allegro 500F Agricultural Fungicide label.

> DO NOT apply during periods of dead calm or when winds are gusty. DO NOT overspray non-target terrestrial or aquatic habitats. DO NOT contaminate aquatic habitats when cleaning and rinsing spray equipment or containers.

Other Information

The relevant test data on which the decision is based (as referenced in this document) are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra_infoserv@hc-sc.gc.ca).

Any person may file a notice of objection[5] regarding this registration decision within 60 days from the date of publication of this Registration Decision document. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the PMRA's website (Requesting a Reconsideration of Decision, www.pmra-arla.gc.ca/english/pubreg/reconsideration-e.html) or contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra_infoserv@hc-sc.gc.ca).

[5] As per subsection 35(1) of the *Pest Control Products Act*.

References

A. LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT

1.0 Chemistry

PMRA #	Reference
1154857	2004, Determination of n-Octanol/Water Partition Coefficient - CAPA, Ricerca 017119-1, DACO: 2.14.1
11243579	1999, Fluazinam (IKF - 1216) - Method Validation [Determination of AI and Related Impurities in Fluazinam (IKF-1216), TGAI by HPLC, Analytical Services, 4039-98-0203-AS-001, DACO: 2.13.1
1260870	Product Chemistry - Fluazinam - Applicant, Manufacturer and Manufacturing Plant Name and Address, DACO: 2.1,2.2
1260871	2005, Description of Beginning Materials and Manufacturing Process Technical Fluazinam (IKF-1216) as Modified - Yokkaichi Plant, Ishihara Sangyo Kaisha, Ltd., 216-04-06102-1, DACO: 2.11.1,2.11.2,2.11.3
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1260873	2005, Discussion of Formation of Impurities Technical Fluazinam (IKF-1216) from Modified Process - Yokkaichi Plant, Ishihara Sangyo Kaisha, Ltd., 216-04-06103-1, DACO: 2.11.4
1260874	2005, Product Identity and Composition / Technical Fluazinam (IKF-1216) from Modified Process - Yokkaichi Plant, Ishihara Sangyo Kaisha, Ltd., 216-04-06101-1, DACO: 2.13.2
1260875	2004, Fluazinam Technical, Analysis of Five Batches (Sample Group 1), 310260.1.029, DACO: 2.13.3
1260876	2000, Fluazinam: Analysis of Twenty (20) Batches from Manufacturing Site in France (SISSA) Using Modified Process, Certified Limits, Ishihara Sangyo Kaisha, Ltd, 216-00-06202-1, DACO: 2.13.3
1260877	2000, Product Identity and Composition / Technical Fluazinam (IKF-1216) from Modified Process, Ishihara Sangyo Kaisha, Ltd., 216-00-06101-3, DACO: 2.13.2

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1260880 2000, Certified Limits Technical Fluazinam (IKF-1216) from Modified Process, Ishihara Sangyo Kaisha, Ltd., 216-00-06202-1, DACO: 2.12.1

2.0 Impact on Human and Animal Health

PMRA # Reference

1154858 2005, Technical Fluazinam: Developmental Neurotoxicity Study in the Rat by Oral (Gavage) Administration., ISK 272/042019, DACO: 4.5.14

3.0 Impact on the Evironment

PMRA # Reference

1154857 2004, Determination of *n*-octanol/water partition coefficient - CAPA. Study No. IB-2004-JLW-003-01-00. Document No. 017119-1.

1154859 2004. A hydrolysis study of [^{14}C]CAPA in water. Document No. 017120-1.

1154860 2006. SDS-67200 - Toxicity to midge (*Chironomus tentans*) during a 10-day sediment exposure. Study No. 13562.6135

1154861 2006. SDS-67200 - Toxicity to freshwater amphipods (*Hyalella azteca*) during a 10-day sediment exposure. Study No. 13562.6136.